UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

Ex parte NAKAYUKI YAMAMOTO and TERUOMI ITO

Appeal No. 2006-2079
Application No. 08/913,056

Heard: November 15, 2006

Before ADAMS, GRIMES, and LEBOVITZ, Administrative Patent Judges.

LEBOVITZ, Administrative Patent Judge.

DECISION ON APPEAL

This appeal involves claims to a preparation for transmucosal administration of physiologically active peptides. The Examiner has rejected the claims as indefinite and obvious. We have jurisdiction under 35 U.S.C. § 134. We affirm.

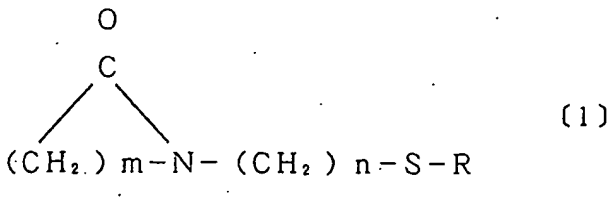
Discussion

Claim construction

Claims 1-27, which are all the pending claims in this application, are on appeal. There are two prior art rejections, of claims 1-27, and of claims 1-3, 18, 19, and 21-27. There is also rejection under § 112, second paragraph, that involves three different terms appearing in claims 3, 11, and 21. The claims stand or fall together in each

rejection. Brief, page 7. Because Appellants chose to argue the claims as a group, we are authorized by 37 C.F.R. § 41.37(c)(1)(vii) to select a single claim from each grouping as representative for deciding each ground of rejection. We select claim 1 as representative of each of the two prior art rejections. Claims 3, 11, and 21 are representative of the rejections under § 112, second paragraph.

> 1. A preparation for transmucosal administration comprising (a) a physiologically active peptide admixed with (b) an absorption promoter having absorption promoting action for the physiologically active peptide on nasal mucosa or rectal mucosa, and (c) a compound having vasodilating activity without mucosal irritation.
>
> 3. The preparation for transmucosal administration according to claim 1 wherein the absorption promoter is a member selected from the group consisting of salt of bile acid, salt of fusidic acid, salt of glycyrrhizic acid, salt of O-acyl-L-carnitine, phospholipid, non-ionic surface active agent, cyclodextrin, higher fatty acid, 1-alkyl-2-pyrrolidone derivative, 1-dodecylazacycloheptane-2-one, bacitracin, sodium azulenesulfonate, azacycloalkane derivative of the formula



(1)

> wherein R is an alkyl, m is an integer of 2-4 and n is an integer of 1-15, provided that R is an alkyl with a carbon number of 5-11 in case where n is 1-3, and mixtures thereof.
>
> 11. The preparation for transmucosal administration according to claim 3 wherein non-ionic surface active agent is a member selected from the group consisting of polyoxyalkylene lauryl, polyoxyalkylene (24) cholesteryl ether, and a mixture thereof.
>
> 21. The preparation for transmucosal administration according to claim 1 wherein the compound having vasodilating activity is admixed with below 1/2 of minimum usual dose as an effective component of the said compound in the preparation for transmucosal administration.

Claim 1 has three elements: a) active peptide; b) an absorption promoter "having absorption promoting action for the physiologically active peptide on nasal mucosa or rectal mucosa"; and c) a compound having vasodilating activity "without mucosal irritation."

The preamble of the claim states that the preparation is "for transmucosal administration." Preamble language that merely states the purpose or intended use of an invention is generally not treated as limiting the scope of the claim. Bicon, Inc. v. Straumann Co., 441 F.3d 945, 952, 78 USPQ2d 1267, 1273 (Fed. Cir. 2006); Boehringer Ingelheim Vetmedica, Inc. v. Schering-Plough Corp., 320 F.3d 1339, 1345, 65 USPQ2d 1961, 1964 (Fed. Cir. 2003). "However, the preamble is regarded as limiting if it recites essential structure that is important to the invention or necessary to give meaning to the claim." Bicon, 441 F.3d at 952, 78 USPQ2d at 1273. Here, the preamble of the claim states that the preparation is intended for transmucosal administration, but does recite any structural features that define the claimed preparation. We do not find the preamble as necessary to give meaning to the claim because the components of the preparation expressly recite limitations that involve transmucosal administration. Accordingly, we do not treat the preamble as limiting the scope of the claim.

The second component of the preparation is an "absorption promoter having absorption promoting action." It is defined in the specification as "a general term for changing biomembrane permeability, increasing up absorbalility [sic] and increasing up bioavailability of the drugs, and has promoting action for absorption of physiologically active peptide on nasal mucosa or rectal mucosa." Specification, page 4. The

absorption promoter is characterized by the claim as having "promoting action" for the peptide on mucosa. In the context of the specification, we construe "promoting action" to mean that the absorption promoter increases the absorption and bioavailability of the peptide when it is applied to the mucosa.

The third component of the preparation is a compound with vasodilating activity which is "without mucosal irritation." The phrase "without mucosal irritation" was added to claim 1 by amendment. Amendment dated May 11, 1999. In introducing it to the claim, Appellants relied on specification disclosure that the claimed preparation was "without detrimental action on the mucosa" (specification, page 4, line 1; page 37) and that the type of vasodilators described in the application (specification, pages 8-9) would "inherently possess the non-irritating nature on the mucosal tissue." Amendment dated May 11, 1999, page 5. Accordingly, we construe the phrase "without mucosal irritation" to mean that the vasodilators are without detrimental action on the mucosa when applied to it.

Obviousness under 35 U.S.C. § 103

1. Masiz and others

Claims 1-27 stand rejected 35 U.S.C. § 103(a) as obvious over Masiz[1] in view of Roberts[2], Azria[3], Kissel[4], Aliverti[5], Alexander[6], Hirai[7], Cooper[8], EPA 115627[9], Nakagawa[10], Masada[11], Hansen[12], and Majeti[13].

Because we have selected claim 1 as representative of the claims grouped together in this rejection, it is unnecessary to consider all the references relied upon by the Examiner in setting forth the complete grounds of rejection. To review the rejection as it pertains to claim 1, we have found it necessary to consider Masiz, Roberts, Cooper, Nakagawa, and Hansen. The remaining references are cited by the Examiner apparently[14] for limitations recited in dependent claims, but not in independent claim 1.

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[1] Masiz, U.S. Patent 5,645,854, Jul. 8, 1997.
[2] Roberts, U.S. Patent 5,750,141, May 12, 1998.
[3] Azria, U.S. Patent 5,149,537, Sep. 22, 1992.
[4] Kissel, "Tolerability and Absorption Enhancement of Intranasally Administered Octreotide by Sodium Taurodihydrofusidate in Healthy Subjects," Pharmaceutical Research, Vol. 9, No. 1, pp 52-57 (1992).
[5] Aliverti, JP 3-5427, Jan. 11, 1991.
[6] Alexander, EP 0215697A2, Mar. 25, 1987.
[7] Hirai, EP 094157A1, Nov. 16, 1983.
[8] Cooper, U.S. Patent 4,557,934, Dec. 10, 1985.
[9] Mufson, EP 0115627A1, Aug. 15, 1984.
[10] Nakagawa, U. S. Patent 4,882,359, Nov. 21, 1989.
[11] Masada, U.S. Patent 5,011,824, Apr. 30, 1991.
[12] Hansen, U.S. Patent 5,120,546, Jun. 9,1992.
[13] Majeti, U.S. Patent 5,599,554, Feb. 4, 1997.
[14] In setting forth the grounds of the rejection, Appellants complain that the Examiner "provides no roadmap as to which references are considered pertinent to which claims, instead applying the references en masse." Brief, pages 7-8. While "brevity is the soul of wit" [W. Shakespeare, Hamlet] in real life, it is not in making a prior art rejection. We refer the examiner to M.P.E.P. § 1207.02 where it is stated: "For each rejection under 35 U.S.C. 102 or 103 where there are questions as to how limitations in the claims correspond to features in the prior art ..., the examiner must compare at least one of the rejected claims feature by feature with the prior art relied on in the rejection. The comparison must align the language of the claim side-by-side with a reference to the specific page, line number, drawing reference number, and quotation from the prior art."

Masiz describes a transdermal delivery device for delivering an active agent to the blood supply which is "constructed of four elements, namely, a vasodilator, a penetration enhancer, the active ingredient, and a water soluble gum." Masiz, column 2, lines 31-35; Abstract.

Roberts teaches compositions for topical and transdermal administration comprising a therapeutic agent and a vaso-active agent (including vasoconstrictors and vasodilators), where the vaso-active agent increases the local and systemic delivery of the therapeutic agent. Roberts, Abstract; column 5, lines 5-13, 53-57; column 7, line 67-column 8, line 4.

Cooper, Nakagawa, and Hansen are each directed to topical or transdermal delivery of drugs. They teach that permeation or penetration enhancers can be utilized in combination with the drug to facilitate delivery through the skin. Cooper, Abstract; column 5, lines 48-51. Nakagawa, Abstract; column 10, line 39-51. Hansen, Abstract; column 7, line 62-column 8, line 37.

The Examiner states that Masiz describes "transdermal delivery comprising a permeation enhancer, a vasodilator, and an active [drug]." Office Action, Paper No. 23, page 2. These elements generically meet the requirements of claim 1 for (a) a peptide ("active"), (b) absorption promoter ("permeation enhancer"), and (c) compound having vasodilating activity ("vasodilator"). Peptides (a) as therapeutic agents are disclosed in Masiz (column 4, line 33), Nakagawa (claim 10), Cooper (column 9, lines 65-67), and Hansen (claim 7). For an absorption promoter "having absorption promoting action for the physiological peptide on ... mucosa," the Examiner cites Cooper, Nakagawa, and Hansen. For a "compound having vasodilating activity without mucosal irritation," the

Examiner cites Roberts. The Examiner concludes that it would have been obvious to have utilized the particular vasodilators and absorption promoters for their known "beneficial" effects. Office Action, Paper No. 23, pages 3-4.

Appellants argue that the vasodilators described by Masiz are "necessarily" irritants which are used "to promote absorption of the active ingredients through the notoriously difficult transdermal route." Brief, page 16, lines 10-11. Because claim 1 requires "a compound having vasodilating activity without mucosal irritation," Appellants assert that there would have been no motivation to have replaced "the irritant vasodilators of [Masiz] with suitable vasodilators for transmucosal administration." Id., page 10. They also argue that there would have been no motivation to have replaced the transdermal permeation enhancers of Masiz with "any of the transmucosal absorption promoters of the remaining ... secondary references." Id., page 11.

"When patentability turns on the question of obviousness, the search for and analysis of the prior art includes evidence relevant to the finding of whether there is a teaching, motivation, or suggestion to select and combine the references relied on as evidence of obviousness." In re Sang Su Lee, 277 F.3d 1338, 1343, 61 USPQ2d 1430, 1433 (Fed. Cir. 2002). A suggestion, teaching, or motivation to combine the relevant prior art teachings does not have to be found explicitly in the prior art. "[T]he teaching, motivation, or suggestion may be implicit from the prior art as a whole, rather than expressly stated in the references. The test for an implicit showing is what the combined teachings, knowledge of one of ordinary skill in the art, and the nature of the problem to be solved as a whole would have suggested to those of ordinary skill in the art." In re Kahn, 441 F.3d 977, 987-988, 78 USPQ2d 1329, 1336 (Fed. Cir. 2006).

Appellants argue that Masiz's teaching is restricted to vasodilators which are counter irritants, while the Examiner takes a broader view. In particular, Appellants assert that because the only vasodilators disclosed in Masiz are counter irritants (Masiz, column 3, lines 28-30), Masiz "necessarily" teaches that only these vasodilators can be used. They assert, but provide no evidence, that counter irritants are necessary "to promote absorption of the active ingredients through the notoriously difficult transdermal route." Brief, page 16, lines 10-11.

We do not find Appellants' argument to be persuasive. Masiz explains that the purpose of the vasodilator in the transdermal delivery device is to increase blood flow to the skin location where the active agent is transferred transdermally into the blood. "[T]he vasodilatory aspect of the MULE [Masiz's delivery device] maximizes blood flow to the transport site so as to reliably maximize absorption of the drug molecule." Id., column 2, lines 43-46.

To enhance blood flow to the skin region where transdermal transfer is to take place, Masiz describes utilizing "a vasodilator and/or topical counter irritant." Id., Abstract; column 2, lines 62-63. The use of the phrase "and/or", which indicates one or the other or both, strongly suggests that Masiz contemplates two classes of agents, each which works to maximize blood flow to the affected area, albeit through different mechanisms. In clarifying the mechanism through which the topical counter irritant works, Masiz again uses the phrase "and/or" to indicate that it is not the only mechanism through which blood flow can be increased to the skin.

> The first element of the MULE is one that enhances blood flow, through vasodilatory action, and/or through counter irritational action at the transport site. For example, topical counter irritants can be used, which are substances that

> provide a mild dermal irritation, generally creating a hot or cold sensation in the area of application. This sensation results from the fact that the mild skin irritation brings blood closer to the surface of the skin, and can be utilized to enhance blood supply and effective transport of the active ingredient/carrier.

Column 2, line 61-column 3, line 3. (Emphasis added.)

Thus, although the only examples disclosed by Masiz are counter irritants, we do not understand Masiz to restrict its teachings to these agents in view of its more general teaching to include a "vasodilatory" activity in its transdermal device in order to maximize blood flow to the skin transport site. Masiz, column 2, lines 43-46.

Further evidence can be found in Roberts who provides methods and compositions for topical and transdermal administration of drugs. Roberts, column 5, lines 7-10. The Roberts patent establishes that the use of vasodilators to enhance the topical delivery of active agents was known in the prior art.

> When vasodilators are used in regard to the composition of the invention they are useful in facilitating local blood flow adjacent a particular tissue site thereby facilitating not only faster delivery of the therapeutic agent but also in higher concentrations.

Roberts, column 6, lines 15-19.

> The use of vasodilators in the composition of the invention is able to increase the rate of systemic absorption of the active compound of interest by enhancing the rate at which it is cleaned from the application site by the local blood supply.

Id., column 7, line 67-column 8, line 4.

Roberts also lists eight specific agents or classes of agents that are "suitable vasodilators" for topical delivery, which include all the compounds "having vasodilating activity without mucosal irritation" listed in appealed claim 19.

Roberts, column 8, lines 5-9:	Claim 19
"Examples of suitable vasodilators include	
[1] lidocaine,	
[2] nitroglycerine,	"nitroglycerin"
[3] and other organic nitrates, or	"isosorbide dinitrate"
[4] glyceryl trinitrate,	
[5] papaverine,	
[6] nicotinates and	
[7] various prostaglandins (more correctly eicosanoids) and	"prostaglandin E1"
[8] various calcium antagonists."	"calcium channel blocker"

Roberts' disclosure does not support Appellants' inference that counter irritants are necessary in Masiz to traverse the "notoriously difficult transdermal route." Brief, page 16, line 11. To the contrary, Roberts teaches vasodilators for transdermal delivery of the same type which Appellants characterize in claim 1 as "having vasodilating activity without mucosal irritation." Robert's description also supports the Examiner's position that a person of ordinary skill in the art would have understood Masiz's teaching to use a vasodilatory activity in a transdermal device was not restricted to counter irritants, but would have included other vasodilators.

Appellants also argue that Masiz does not disclose or suggest "transmucosal absorption promoters required by the present claims." Brief, page 8. However, Masiz discloses permeation or penetration enhancers (Masiz, column 3, lines 30-33) which increase a compound's absorption, consistent with our construction of "absorption promoter" and "promoting action." The Examiner cited several references, including Nakagawa (column 10, lines 21-26), Hansen (column 8, lines 5-6), and Cooper (abstract) for teaching absorption promoters (permeation enhancers) for topical application which are of the same type disclosed and claimed in the instant application.

All three[15] of the cited patents describe transdermal delivery, the same route utilized by Masiz and Roberts.

The use of penetration enhancers to increase transdermal delivery of a therapeutic agent was known prior to the filing date of the instant application. Masiz states that penetration enhancers had been used in the prior art to facilitate transdermal delivery of drug molecules. Masiz, column 1, lines 55-64. Each of Cooper, Nakagawa, and Hansen confirm that penetration enhancers were recognized in the art as beneficial for topical delivery of drugs. See above. Accordingly, a person of ordinary skill in the art would have viewed the inclusion of penetration enhancers in a topical delivery device as conventional, and would not have restricted Masiz's device to the particular penetration enhancers disclosed in it, but would have recognized that other prior art penetration enhancers could be utilized, including the agents described in Nakagawa, Hansen, and Cooper. Appellants have not distinguished the claimed "absorption promoter" from the penetration enhancers described in the prior art.

According to Appellants, "a critical shortcoming" of Masiz is that it "contemplates solely transdermal delivery ... and therefore not only fails to disclose or suggest the claimed vasodilators and absorption promoters suitable for transmucosal delivery, but also destroys any motivation to substitute components selected from use in one type of administration system, for use in an entirely different administration route." Brief, page 11. We do find this argument persuasive because each of Masiz, Roberts, Cooper,

[15] On page 9, line 8-11 of the Appeal Brief, it is stated that Nakagawa describes compositions for transmucosal administration. However, we find clear disclosure in Nakagawa of compositions intended for transdermal delivery. Column 1, lines 59-66; column 2, lines 3-26; column 10, lines 39-44; column 23, lines 1-40. At column 25, line 24-column 26, line 42, a topical composition containing drug is applied to the skin and the presence of the drug in the blood serum is subsequently measured, showing that transdermal administration is effective.

Nakagawa, and Hansen describe the same administration route. The limitations in claim 1 that the absorption promoter and vasodilatory compound have certain properties when used for transmucosal delivery have not been ignored; rather, we have found these limitations to have been met by the prior art, despite the fact the prior art relates to transdermal delivery.

For the foregoing reasons, we find that the Examiner has set forth adequate evidence to establish prima facie obviousness of claim 1. Because claims 2-26 were not separately argued, they fall together with claim 1.

2. Gyory, Sage, and Haak

Claims 1-3, 18, 19, and 21-27 stand rejected under 35 U.S.C. § 103(a) as obvious over Gyory[16] in view of Sage[17] and Haak.[18]

All three cited patents teach the delivery of drugs, including peptides, using iontophoresis. Sage describes combining an active agent with an enhancing amount of a vasodilator. Sage, Abstract; column 2, lines 62-65. Haak describes selecting an optimal site for iontophoretic delivery of a drug. Haak, Abstract; column 4, lines 30-33. According to Haak, skin permeation enhancers can be utilized with the drug. Id., column 7, lines 3-5. Gyory teaches a two phase adhesive matrix for use in an iontophoretic delivery device. Gyory, Abstract. It can be used to adhere the device to the skin or mucosa. Id.

Having identified all elements of the claimed subject matter in the prior art, the Examiner concludes that a person of ordinary skill in the art would have found it obvious

[16] Gyory, U.S. Patent 5,240,995, Aug. 31, 1993
[17] Sage, U.S. Patent 5,302,172, Apr. 12, 1994
[18] Haak, U.S. Patent 5,167,616, Dec. 1, 1992

to have combined the agents described in each of the references for their known benefit ("to enhance delivery") in facilitating the iontophoretic delivery of drugs. Office Action, Paper No. 23, page 6.

Appellants argue that Sage "teaches that ... the vasodilator tolazoline enhances the transdermal delivery of lidocaine [which is] not a peptide, although certain peptides are mentioned" in a long list of other possible ingredients. Brief, page 18. They also assert that Haak "relates to a discovery that iontophoretic delivery of drugs surprisingly occurs more readily when applied to intact back skin." Id. "The nature of the drug ... is not pertinent ... although peptide are mentioned." Id. Finally, Appellants conclude the attempt to reconstruct the claimed subject matter is an exercise in impermissible hindsight. Id., page 19.

In reaching an obviousness determination, it is necessary to identify the differences between the claimed invention and the prior art, and then to determine whether these differences are obvious in view of the scope and content of the prior art and the level of skill in the pertinent art. Graham v. John Deere Co., 383 U.S. 1, 13-14, 148 USPQ 459, 465 (1966). The cited prior art does not describe the combination of a vasodilator and absorption promoter, but the Examiner considers it obvious to have combined them for their known advantage in enhancing the delivery of drugs. We do not find a flaw with this reasoning. A skilled worker is normally motivated to improve what is already known. Haak's suggestion to deliver a drug with a skin permeation enhancer (column 7, lines 3-4) was not in the context of a particular drug or composition, but would have been recognized by the skilled worker as generally teaching its value for iontophoretic drug delivery. Appellants conclude that it is

"impermissible hindsight" (Brief, page 19) to add Haak's permeation enhancer to Sage's drug/vasodilator composition, but do not explain why it is hindsight to follow an explicit suggestion in the art to use an absorption promoter.

We also do not agree with Appellants' characterization of Sage's disclosure as being restricted to the combination of tolazoline and lidocaine. The patent discloses this combination as a "preferred composition," but it more generally describes its "invention" as a vasodilator and active agent. Sage, column 2, lines 20-30 ("Summary of the Invention"). The vasodilators described by Sage "can be selected from the major categories of vasodilators generally referred to as cerebral, coronary and peripheral." Id., column 7, lines 15-18. Appellants have not challenged the Examiner's presumption that such vasodilators satisfy the requirement of claim 1 of "having vasodilating activity without mucosal irritation." However, they find fault with the Examiner's statement that "[i]t would have been obvious ... to add a vasodilator to the vehicle of Sage" (Office action dated Nov. 26, 2002, Paper No. 23) because Sage was cited for its teaching of a vasodilator, not a vehicle. Brief, pages 18-19. We agree with Appellants that the Examiner made a misstatement in describing Sage's disclosure; however, because the Examiner on the same page correctly characterizes Sage as teaching a vasodilator, we do not find that this misstatement would have misled Appellants as to the basis of the rejection.

The Examiner relies on Sage and Haak for administration of peptides. With respect to Haak, Appellants minimize its disclosure of peptides, stating that "peptides are mentioned in the passage at column 6, lines 36-38." Id., page 18. In fact, Haak states that "[m]ore preferably, the invention is useful in the controlled delivery of

peptides." Id. Accordingly, in view of the evidence that all three cited references describe peptide drugs, we concur with the Examiner that administration of a peptide would have been obvious to the skilled worker as a drug which is conventionally administered by iontophoresis.

In sum, we conclude that adequate evidence has been presented to establish prima facie obviousness of claim 1. Because claims 2, 3, 18, 19, and 21-27 were not separately argued, they fall together with claim 1.

In concluding that prima facie obviousness has been established, we find it unnecessary to rely on Gyory. The Examiner cited Gyory for its teaching of "iontophoretic delivery on a mucosal membrane," but did not state whether it was applied to independent claim 1 or other dependent claims grouped in the same rejection. Office Action, Paper No. 23, page 6.

Indefiniteness under § 112, second paragraph

Claims 3-17 and 21 stand rejected under 35 U.S.C. § 112, second paragraph as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as his invention.

The Examiner makes the following objections to the claim language (Office action, page 6):

1) Claim 3: The term "higher" in the context of "higher fatty acid" is vague because it is "subjective." It does not state the specific carbon atom range present in a higher fatty acid. Brief, page 20.

2) Claim 11: The term "polyoxyhethylene [polyoxyalkylene, sic] laurel" is indefinite because it is not clear whether "an ether or ester" is claimed.

3) Claim 21: The term "usual" in claim 21 in the context of "1/2 of minimum usual dose of an effective component" is vague because it is subjective.

The definiteness requirement of 35 U.S.C. § 112, second paragraph, "is essentially a requirement for precision and definiteness of claim language." PPG Industries, Inc. v. Guardian Industries Corp., 75 F.3d 1558, 1562, 37 USPQ2d 1618, 1621 (Fed. Cir. 1996) (quoting from In re Borkowski, 422 F.2d 904, 909, 164 USPQ 642, 646 (CCPA 1970). The language of the claims must make it clear what subject matter they encompass to provide adequate notice to "accurately determine the boundaries of protection involved and evaluate the possibility of infringement and dominance." In re Hammack, 427 F.2d 1378, 1382, 166 USPQ 204, 208 (CCPA 1970). A claim is considered indefinite if it does not reasonably apprise those skilled in the art of its scope. Amgen, Inc. v. Chugai Pharm. Co., 927 F.2d 1200, 1217, 18 USPQ2d 1016, 1030 (Fed. Cir. 1991); IPXL Holdings, LLC. v. Amazon.com, Inc., 430 F.3d 1377, 1383-1384, 77 USPQ2d 1140, 1145 (Fed. Cir. 2005).

1) "higher fatty acid"

We agree with the Examiner that the term "higher" does not reasonably apprise the skilled worker as to what fatty acids would be covered by the claim. Appellants refer to a search of the USPTO full-text database which shows that the "identical phrase 'higher fatty acid' or 'higher fatty acids' appears in the claims of fully 1074 U.S. patents issued since 1976." Brief, page 20. We do not find this argument persuasive. First, Appellants have not provided the search relied upon to reach this conclusion.

Consequently, we do not have this evidence before us. Secondly, we remind Appellants that claims are read in view of the specification of which they are part. Phillips v. AWH Corp., 415 F.3d 1303, 1315, 75 USPQ2d 1321, 1327 (Fed. Cir. 2005). Consequently, a determination that a certain claim term in a patent is definite, does not necessarily lead to the conclusion that the same term in the context of a different patent (or patent application) would also be definite. Appellants did not identify support for the phrase in the instant specification nor explain why it would reasonably apprise the skilled worker of its scope.

2) "polyoxyhethylene laurel"

We agree with the Examiner that, because of the claim's grammatical construction, it is unclear whether a "polyoxyalkylene lauryl" ether or ester is claimed. Office Action, Paper No. 23, page 6. Consequently, we affirm the rejection with respect to this claim.

3) "1/2 of minimum usual dose of an effective component"

Appellants argue that the "use of the term 'usual' in the context of the minimum conventional dose of an active ingredient is ... appropriate [because] ... the particular amount will vary based on the identity of the active ingredient." Brief, page 22.

Claim 21 requires that the dosage be "below 1/2 of the minimum usual dose" of the compound having vasodilatory activity. We find the claim indefinite because it does not identify the administration route in which the dose is "usual," i.e., transmucosal, oral, parenteral, etc., nor whether it is "usual" with respect to a particular patient or patient class. Consequently, we affirm the rejection with respect to this claim.

In sum, we affirm the rejection of claims 3-17 and 21 under 35 U.S.C. § 112, second paragraph.

No time period for taking any subsequent action in connection with this appeal may be extended under 37 CFR § 1.136(a).

AFFIRMED

Eric Grimes
Administrative Patent Judge

Richard M. Lebovitz
Administrative Patent Judge

) BOARD OF PATENT
) APPEALS AND
) INTERFERENCES

ADAMS, Administrative Patent Judge, dissenting-in-part.

I agree with my colleagues in that claims 3-17 and 21 are indefinite under 35 U.S.C. § 112, second paragraph and that claim 1[19] is unpatentable under 35 U.S.C. § 103(a) as obvious over the combination of Gyory, Sage and Haak. However, for the reasons set forth below, I cannot join with the Majority's conclusion that the combination of Masiz, Roberts, Azria, Kissel, Aliverti, Alexander, Hirai, Cooper, EPA 115627, Nakagawa, Masada, Hansen and Majeti supports the rejection of claims 1-27 under 35 U.S.C. § 103(a).

Claim construction:

Claims 2-27 depend directly or indirectly from claim 1. Accordingly, I focus attention on claim 1. As the Majority recognizes (supra, page 2), claim 1 is directed to:

> A preparation for transmucosal administration comprising (a) a physiologically active peptide admixed with (b) an absorption promoter having absorption promoting action for the physiologically active peptide on nasal mucosa or rectal mucosa, and (c) a compound having vasodilating activity without mucosal irritation.

I agree with the Majority's finding that the preamble of claim 1 does not limit the scope of the claimed composition. See supra, page 3. Therefore, as the Majority emphasizes (Id.), the composition of claim 1 comprises three elements, specifically:

> a) an active peptide;
>
> b) an absorption promoter "having absorption promoting action for the physiologically active peptide on nasal mucosa or rectal mucosa"; and

[19] As the Majority correctly observes (supra, page 15), claims 2-3, 18, 19, and 21-27 fall together with claim 1.

c) a compound having vasodilating activity "without mucosal irritation."

Regarding the second element of the claimed composition, I agree with the Majority's construction of the term "'promoting action' to mean that the absorption promoter increases the absorption and bioavailability of the peptide when it is applied to the mucosa." Supra, page 4. Regarding the third element of Appellants' claimed composition, I agree with the Majority's construction of the phrase "without mucosal irritation" to mean that the vasodilators do not detrimentally affect (e.g. irritate) the mucosa. Id.

Therefore, to meet the requirements of Appellants' claimed composition a prior art composition must comprise, inter alia, a compound that has vasodilating activity without irritating the mucosa. Contrary to the Majority's conclusion (supra, pages 5-12), the combination of "Masiz and others" does suggest this composition to a person of ordinary skill in the art at the time the invention was made.

The combination of "Masiz and others":

As the Majority correctly points out (supra, page 6), "Masiz describes a transdermal delivery device for delivering an active agent to the blood supply which is 'constructed of four elements, namely, a vasodilator, a penetration enhancer, the active ingredient, and a water soluble gum.' Masiz, column 2, lines 31-35; Abstract." Therefore, at first blush the Majority appears to be correct in their finding that the composition disclosed by Masiz "generically meet[s]" the requirements of Appellants' claim 1. Supra, page 6. However, focusing solely on the vasodilator component of

Masiz's composition, I disagree with the Majority's intimation that Masiz would suggest the use of a vasodilator that does not cause mucosal irritation as is required by Appellants' claimed invention.

As the Majority recognizes (supra, page 8),

> Masiz explains that the purpose of the vasodilator in the transdermal delivery device is to increase blood flow to the skin location where the active agent is transferred transdermally into the blood. . . .
> To enhance blood flow to the skin region where transdermal transfer is to take place, Masiz describes utilizing "a vasodilator and/or topical counter irritant."

Recognizing Masiz's disclosure of "a vasodilator and/or topical counter irritant" to enhance blood flow to the skin, the Majority goes into some detail on the use of the phrase "and/or" intimating that the use of the phrase "and/or" "strongly suggests that Masiz contemplates two classes of agents each which works to maximize blood flow to the affected area, albeit through different mechanisms." Supra, page 8, emphasis added.

Therefore, as I understand the Majority opinion, while Masiz describes a composition that comprises a vasodilator (see supra page 6), the vasodilator may be substituted for, or used in conjunction with, a different class of agent known as a "topical counter irritant," which achieves the same effect as the vasodilator but operates through a different mechanism (see supra, page 8). Masiz does not support this reasoning. Instead, Masiz expressly discloses that "[s]uitable vasodilators or counter irritants include menthol, methyl salicylate, oil of wintergreen, peppermint oil, and capsisium, with menthol being preferred." Column 3, lines 28-30. Therefore, instead of describing two classes of agents as the Majority would lead us to believe, Masiz expressly

discloses vasodilators and counter irritants as comprising the same class of agents, which operate through the same mechanism. No doubt, the list of "suitable" agents set forth in Masiz is not exhaustive and giving the Majority the benefit of the doubt that Masiz discloses a genus of potentially suitable vasodilators[20], the question remains – why would a person of ordinary skill in the art select only those vasodilators that do not cause mucosal irritation?

To answer this question the Majority looks to Appellants' claimed invention (e.g., claim 19), and compares the specific vasodilators listed therein with a listing of "suitable vasodilators" in Roberts. Tabulating the results of their effort in a table at page 9 of their opinion, the Majority finds that of the genus of vasodilators taught by Roberts four are the same as set forth in Appellants' claim 19. From this analysis, the Majority finds (supra, page 10), "Roberts teaches vasodilators for transdermal delivery of the same type which Appellants characterize in claim 1 as 'having vasodilating activity without mucosal irritation.'" Therefore, the Majority concludes "[t]he limitations in claim 1 that the . . . vasodilatory compound have certain properties when used for transmucosal delivery have not been ignored; rather, we have found these limitations to have been met by the prior art . . . ." Supra page 12.

In my opinion, this reasoning relies on the hindsight reconstruction that the courts have condemned. See Dembiczak, 175 F.3d at 999, 50 USPQ2d at 1617 ("Combining prior art references without evidence of such a suggestion, teaching, or motivation

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[20] See supra, page 10, "a person of ordinary skill in the art would have understood Masiz's teaching to use a vasodilatory activity in a transdermal device was not restricted to counter irritants, but would have included other vasodilators." See also, supra, page 9, "although the only examples disclosed by Masiz are counter irritants, we do not understand Masiz to restrict his teachings to these agents in view of its more general teaching to include a 'vasodilatory' activity in its transdermal device in order to maximize blood flow to the skin transport site."

simply takes the inventor's disclosure as a blueprint for piecing together the prior art to defeat patentability—the essence of hindsight.").

At best, the cited references, viewed without the benefit of the present disclosure teach the use of vasodilators generically. No doubt, vasodilators that do not cause mucosal irritation are known to those of ordinary skill in the art. However, I do not find, and neither the Examiner nor the Majority have pointed out where any of the references relied upon in this ground to rejection direct a person of ordinary skill in the art to select as the vasodilator of Masiz's composition only those vasodilators that do not cause mucosal irritation. To the contrary, a fair reading of Masiz suggests the opposite, e.g., the use of a vasodilator that has irritating properties.[21]

While a person of ordinary skill in the art may possess the requisite knowledge and ability to modify the composition of Masiz, the modification is not obvious unless the prior art suggested the desirability of the modification. In re Gordon, 733 F.2d 900, 902, 211 USPQ 1125, 1127 (Fed. Cir. 1984). In my opinion, viewed without the benefit of hindsight, the references would not have suggested modifying Masiz's composition in a way that would produce the composition claimed here.

Patentability is determined based on a preponderance of the evidence. See In re Oetiker, 977 F.2d 1443, 1446, 24 USPQ2d 1443,1445 (Fed. Cir. 1992) ("[T]he conclusion of obviousness vel non is based on the preponderance of evidence and argument in the record."). In my opinion, neither the Examiner nor the Majority provide evidence or reasoning to show, by a preponderance of the evidence, that the cited

[21] See e.g., Masiz, column 3, lines 28-30, wherein Masiz expressly discloses that "[s]uitable vasodilators or counter irritants include menthol, methyl salicylate, oil of wintergreen, peppermint oil, and capsisium, with menthol being preferred."

references would have suggested the instantly claimed composition to those of ordinary skill in the art. Therefore, I would reverse the rejection of claims 1-27 under 35 U.S.C. § 103(a) as being unpatentable over the combination of Masiz, Roberts, Azria, Kissel, Aliverti, Alexander, Hirai, Cooper, EPA 115627, Nakagawa, Masada, Hansen and Majeti.

For clarity, I note that the rejection of claims 1-3, 18, 19, and 21-27 under 35 U.S.C. § 103(a) as obvious over the combination of Gyory, Sage and Haak stands on a different footing. In contrast to the rejection over the combination of Masiz, Roberts, Azria, Kissel, Aliverti, Alexander, Hirai, Cooper, EPA 115627, Nakagawa, Masada, Hansen, and Majeti, there is nothing on this record to suggest that the vasodilators taught by Gyory, Sage and Haak cause mucosal irritation.[22]

Dissenting-in-part

Donald E. Adams
Administrative Patent Judge

) BOARD OF PATENT
)
) APPEALS AND
)
) INTERFERENCES
)

[22] See e.g., supra, page 13, wherein the Majority correctly finds "Appellants have not challenged the Examiner's presumption that such vasodilators satisfy the requirement of claim 1 of 'having vasodilating activity without mucosal irritation.'"

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